Prevalence of HIV-1 in Blood Donations Following Implementation of a Structured Blood Safety Policy in South Africa

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S OUTH AFRICA IS IN THE MIDST of an escalating human immunodeficiency virus (HIV)–AIDS pandemic with an estimated 5.3 million people infected.[1] The prevalence of HIV-1 in women attending public antenatal care reached 27.9% in 2003, while 11.4% of the overall population is infected,[2,3] predominantly through heterosexual and perinatal transmission. Although all sectors of the population are affected, there are significant associations with age, race, geography, and sex.[3] In this environment, the South African National Blood Service (SANBS) collects more than 700 000 units of whole blood each year using internationally endorsed principles of voluntary donation, donor screening based on locally determined risk factors, and universal testing for HIV-1 and 2, hepatitis B and C, and syphilis.

The 1990s witnessed a dramatic increase in HIV-1 prevalence culminat-

Context The South African National Blood Service collects more than 700 000 units of blood annually from a population in which 11.4% is infected with human immunodeficiency virus 1 (HIV-1). The prevalence of HIV-1 in blood donations increased to 0.26% (1:385) in 1998, indicating that a significant number of window-period infective units were entering the blood supply (risk 3.4/100 000).

Objectives To determine whether the implementation of a new donor selection policy and educational program introduced in 1999 was associated with reductions in the incidence and prevalence of HIV-1 in blood donations and the reduced transmission risk.

Design We compared the prevalence of HIV-1 in 880 534 blood donations collected from 1999 through 2000 with the 791 639 blood donations collected from 2001 through 2002. We estimated the incidence of HIV-1 in 93 378 (1999-2000) and 67 231 (2001-2002) first-time donations and the residual risk for all donations in 2001-2002 using the less-sensitive enzyme-linked immunoassay and incidence-window period model.

Setting All blood donors in the Inland region of the South African National Blood Service were analyzed.

Intervention Donor clinics in high HIV prevalence areas were closed. Programs targeting repeat donors and youth were initiated and HIV risk behavior education programs were developed. Structured donor interviews and an enhanced donor self-exclusion questionnaire were institutionalized.

Results The prevalence of HIV-1 in blood donations declined from 0.17% in 1999-2000 to 0.08% in 2001-2002 after the implementation of the new donor selection and education policy. The number of high-risk donations collected decreased from 2.6% to 1.7% (P<.001), and the likelihood of these donations being infected decreased from 4.8% to 3.25%. The likelihood of first-time donors being recently infected with HIV-1 decreased from 18% to 14% (P = .07) and respective incidence of high-risk donations collected decreased from 2.6% to 1.7%. Donations from the majority black population declined from 6.6% to 4.2% (P<.001). Analysis of HIV-1 incidence in 2001-2002 suggests a residual risk of collecting a window period infectious unit of 2.6/100 000.

Conclusion The implementation of enhanced education and selection policies in South Africa was associated with decreased prevalence of HIV-1 in blood donations.

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Figure 1. Prevalence of Human Immunodeficiency Virus 1 (HIV-1) Infection in Blood Donations and Attendees of Public Antenatal Clinics
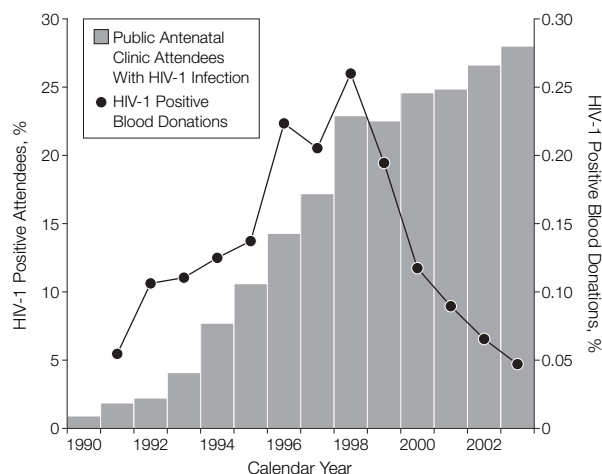
Public antenatal clinic attendees represent a high-risk group for HIV-1 infection in South Africa and provide the only reliable source of annual data on HIV-1 prevalence over a broad geography.[2,23] The data on HIV-1 prevalence in blood donations is unpublished data from the South African National Blood Service.

ing in 1998 when 0.26% (1:385) of blood donations were confirmed with positive results[1] (SANBS, unpublished data, December 2003) (**FIGURE 1**). An analysis of 19 709 donors in 1999 estimated the residual risk of HIV-1 infection at 3.4 per 100 000 donations, implying that 24 infectious units entered the blood supply that year.[4] These data necessitated the introduction of a structured risk-management program to minimize the impact of the escalating HIV pandemic. Enhanced donor selection, education, and product triage procedures were implemented, and rigorous standard operating procedures were enforced, with continued sensitive donor testing for HIV-1 antibodies and the p24 antigen.

We report on HIV-1 prevalence in blood donations before and after implementation of these policies and estimate the residual risk for all blood donations following full program implementation. Our report forms a baseline from which alternate strategies are being implemented that may allow the majority of South Africans to donate blood while sustaining a safe and available supply.

METHODS
Serological Screening and Estimation of HIV Incidence and Residual Risk

A total of 880 534 donations of whole blood and platelets collected between January 8, 1999, and August 8, 2000, and 791 639 units between January 1, 2001, and July 4, 2002 in the Inland region of SANBS were analyzed. All donations were voluntary, nonremunerated, and screened for HIV-1 and 2 antibodies, p24 antigens, hepatitis C antibody, and hepatitis B surface antigen (Abbott Prism, Abbott Park, Ill), and syphilis (Shield Diagnostics, Dundee, Scotland). Repeatedly reactive samples for HIV-1 p24 antigen were confirmed by neutralization (INNOTEST HIV antigen mAb Neutralization, Innogenetics, Belgium) and for HIV-1 and 2 antibody were confirmed using a second enzyme-linked immunoassay (EIA) (HIV-1/HIV-2 Ab-capture, Ortho-Clinical Diagnostics, Raritan, NJ). Human immunodeficiency virus Western blotting was not routinely performed.

The incidence and residual risk of an HIV-1 infectious donation (ie, the risk of collecting an HIV-1 infectious unit despite donor selection and serologi-

cal screening efforts) was estimated using the incidence window period model,[5-10] based on the detection of recent infection by the less-sensitive EIA testing strategy.[11-14] Samples that had tested repeatedly reactive for HIV-1or 2 antibody by 2 EIAs were anonymized (ie, relabeled with a study code linked to demographic and donation information), sent to Blood Systems Research Institute (San Francisco, Calif) and tested by the Standardized Testing Algorithm for Recent HIV Seroconversion (STARHS) protocol. STARHS is based on the detection of low avidity or titer antibodies by a less-sensitive EIA[10] (Vironostika HIV-1 Microelisa, bioMérieux, Durham, NC). Samples that tested negative or weakly reactive by less-sensitive EIA were confirmed using a sensitive EIA (Vironostika HIV-1 Microelisa) and Western blot (Calypte Biotech, Alameda, Calif) to exclude false-positives. The less-sensitive EIA and sensitive EIA are the same assay run under different operating conditions with respect to incubation periods and sample dilution. The HIV-1 incidence and residual risk are estimated using the less-sensitive EIA seroconversion period for HIV-1 clade C infections of 311 days (95% confidence interval, [CI], 217-483).[4,10]

All study participants gave written informed consent for infectious disease testing, including HIV-1 testing, and for inclusion in research studies relating to blood safety. The study was approved by institutional review boards at SANBS and the University of California, San Francisco.

Blood Safety Policy

SANBS and its predecessor blood transfusion services have historically operated as independent nonprofit organizations licensed by the South African Department of Health and entrusted with maintaining a safe and available blood supply for all South Africans. Policies and procedures are vetted by an independent board of directors elected and represented predominantly by blood donors. The SANBS Blood Safety Policy introduced in 1999

is based on procuring sufficient blood for the needs of all patients from low-risk, voluntary donors.[15-18] Donor clinics in areas where HIV prevalence is high were closed and programs targeting the youth and promoting repeat donation were initiated. Risk behavior education programs were developed for staff and donors. These took the form of educational sessions at donor sites and written material given to donors before each donation.

Structured donor interviews with direct oral questioning were institutionalized to ensure understanding of the self-exclusion questionnaire[19] that included questions relating to test-seeking behavior, male sex with males, injection drug abuse, recent sexually transmitted diseases, sex with prostitutes, heterosexual exposure to multiple partners, casual sex, and sexual assault. These are universally accepted criteria for donor deferral, with the additional criteria that donors with a history of sexual assault in the prior 12 months, a history of having more than 1 sexual partner, or having casual sex in the prior 6 months are deferred from donation. All donations were triaged according to a risk profile (**FIGURE 2**) and issued according to a safety hierarchy.

Donation risk profiles were derived from a multivariate analysis performed in 1998 on available demographic markers from 506 953 donations collected between April 1996 and March 1997. Donor HIV-1 prevalence rates were calculated for cohorts defined by sex (male or female); donation site (mobile or fixed clinics); race (white, black, Asian, and mixed race); and donation type (first-time, lapsed, and repeat). First-time donors had no donation record; lapsed donors had not donated in 12 months; and repeat donors had donated within 12 months. Race group was self-identified by the blood donor using using categories defined in the 2001 South African National Census.[20,21] The significant risk indicators ($P<.001$) derived from the model were race group ($\chi^2=1172.21$); sex ($\chi^2=58.68$); location of blood col-

Figure 2. The Prevalence of Human Immunodeficiency Virus 1 (HIV-1) Infection in South African Blood Donations
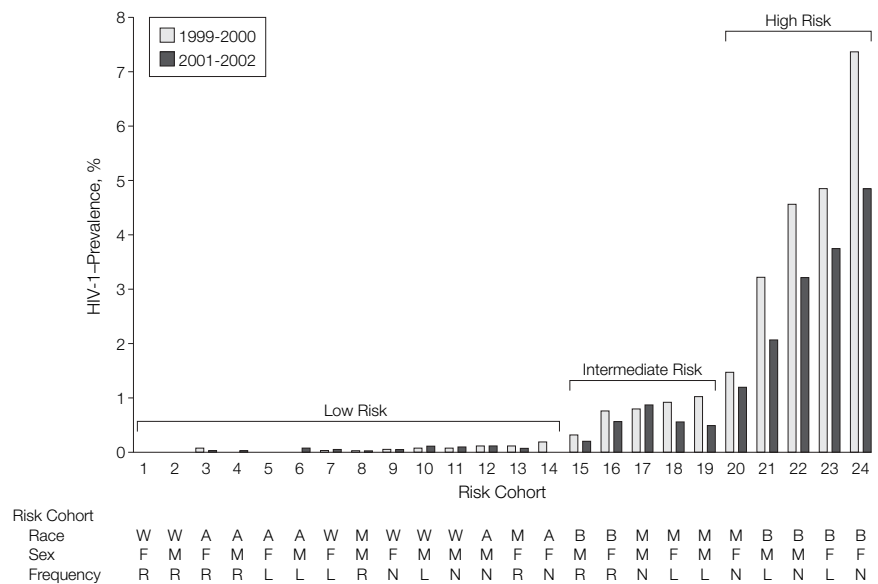
A indicates Asian; B, black; L, lapsed donor; M, mixed race; N, new donor; R, repeat donor; and W, white. Based on unpublished data from the South African National Blood Service.

lection site ($\chi^2=88.13$); and donation type ($\chi^2=164.99$). Risk cohorts were ranked according to HIV-1 prevalence (low $<0.1\%$, intermediate, 0.1%-0.99%, or high risk $\geq1.0\%$). Plasma from all donors was quarantined and only issued for transfusion after an acceptable subsequent donation. Excess plasma was used for fractionation. Cellular components were routinely prepared from low-risk donations. Cellular products from intermediate risk donations were only made available during times of blood shortages.

Statistical Analysis

Comparisons of prevalence rates were performed by logistic regression (version 9.1.3, SAS Institute, Cary, NC). Risk ratio (RR) and odds ratio (OR) were computed over total donations and stratified by demographic variables. Residual risks and yields were estimated using the window period/incidence rate model.[10] Wald-type 95% confidence intervals (CIs) around estimates were computed using a Taylor[22] series approximation of the corresponding SE estimate.

RESULTS
Prevalence of HIV-1 in
South African Blood Donors.

Between 1991 and 1998, the prevalence of HIV-1 in blood donations increased from 0.06% (1:1666) to a peak of 0.26% (1:385)(Figure 1). In 1999, SANBS introduced a new safety policy aimed at improving the South African blood supply. The prevalence rates of HIV-1 decreased after implementation, reaching 0.05% in 2003. In the same period, the HIV-1 prevalence in patients visiting public antenatal clinics over a broad geography increased steadily from 0.7% in 1990 to 27.9% in 2003.[23]

To better understand the decline in prevalence of HIV-1 from donors, we compared the demographics of all collections in the Inland Region of SANBS in corresponding periods of 1999-2000 and 2001-2002. Demographic analysis in 1999-2000 confirmed that HIV-1 was most prevalent in first-time, female, black blood donors, aged 20 to 39 years (**TABLE 1** and Figure 2). Prevalence of HIV ranged from 0.06% to 0.33% in the 6 geographical prov-

inces studied. Overall prevalence declined 50%, from 0.17% in 1999-2000 to 0.08% in 2001-2002 (OR, 2.0; 95% CI, 1.9-2.0; Table 1) with a reduction seen in most demographic groups. This decrease was attributable to a reduction in the proportion of intermediate (4.9% vs 3.3%, $P=.001$) and high-risk (2.6% vs 1.7%, $P<.001$) donations and decreased prevalence in these categories, as defined by sex, donation frequency, and race in our prior multi-variate risk analysis (Figure 2). The low-risk group, incorporating the majority of donors (95% in 2001-2002), showed no change in prevalence.

Incidence of HIV-1 in First-Time Blood Donors

We investigated HIV-1 incidence in first-time donors who yield the majority of infected donations (Table 1). There were 93 378 first-time donors during 1999-2000 and 67 231 in 2001/

2002, representing 10.6% and 8.5%, respectively, of donations, a significant decline ($P<.001$). The prevalence of HIV-1 in first-time donors decreased from 1.08% to 0.59%, representing a 45% decline (OR, 1.8; 95% CI, 1.6-2.1; TABLE 2). All available HIV-seropositive samples from 1999-2000 (674 of 1006) and 2001-2002 (379 of 398) were anonymized and tested in the less-sensitive EIA system to detect recently infected

Table 1. Donor Demographics and Prevalence of Human Immunodeficiency Virus 1 Infection in the Years 1999-2000 and 2001-2002

| | Donation Period | | | | | | | | Comparing HIV Prevalence Between 1999-2000 and 2001-2002 |
| | 1999-2000 | | | | 2001-2002 | | | | |
	No. of Donations	Total Donations, %	HIV Positive	Prevalence, %	No. of Donations	Total Donations, %	HIV Positive	Prevalence, %	Odds Ratio (95% CI)
Total	880 534		1473	0.17	791 639		664	0.08	2.0 (1.9-2.1)
Donation frequency									
First-time	93 378	10.6	1006	1.08	67 231	8.5	398	0.59	1.8 (1.6-2.1)
Lapsed	72 051	8.2	236	0.33	67 262	8.5	159	0.24	1.4 (1.1-1.7)
Repeat	715 105	81.2	231	0.03	657 150	83.0	107	0.02	2.0 (1.6-2.5)
Sex									
Men	560 333	63.6	662	0.12	497 696	62.9	319	0.06	1.8 (1.6-2.1)
Women	320 201	36.4	811	0.25	293 943	37.1	345	0.12	2.2 (1.9-2.5)
Race									
Black	58 169	6.6	1262	2.17	33 222	4.2	484	1.46	1.5 (1.3-1.7)
Mixed	30 768	3.5	104	0.34	24 166	3.1	63	0.26	1.3 (0.9-1.8)
Asian	17 802	2.0	6	0.03	18 559	2.3	6	0.03	1.0 (0.3-3.2)
White	773 794	87.9	101	0.01	715 696	90.4	111	0.02	0.8 (0.6-1.1)
Geography									
Free state	125 229	14.2	221	0.18	106 546	13.5	81	0.08	2.3 (1.8-3.0)
Gauteng	506 194	57.5	760	0.15	441 516	55.8	366	0.08	1.8 (1.6-2.1)
Mpumalanga	125 441	14.2	200	0.16	114 263	14.4	111	0.10	1.6 (1.3-2.1)
Northern Cape	41 594	4.7	26	0.06	37 131	4.7	22	0.06	1.1 (0.6-1.9)
Northern Province	4986	0.6	9	0.18	28 684	3.6	17	0.06	3.0 (1.4-6.8)
North West	77 090	8.8	257	0.33	63 505	8.0	67	0.11	3.2 (2.4-4.1)
Age, y									
16-19	125 753	14.3	170	0.14	108 886	13.8	60	0.06	2.5 (1.8-3.3)
20-24	117 682	13.4	329	0.28	94 602	12.0	116	0.12	2.3 (1.8-2.6)
25-29	111 394	12.7	374	0.34	90 450	11.4	166	0.18	1.8 (1.5-2.2)
30-34	97 380	11.1	271	0.28	89 573	11.3	119	0.13	2.1 (1.7-2.6)
35-39	94 317	10.7	164	0.17	82 748	10.5	93	0.11	1.5 (1.2-2.0)
40-44	93 750	10.6	78	0.08	85 236	10.8	51	0.06	1.4 (1.0-2.0)
45-49	78 796	8.9	48	0.06	76 788	9.7	28	0.04	1.7 (1.0-2.7)
50-54	62 473	7.1	23	0.04	61 155	7.7	17	0.03	1.3 (0.7-2.5)
55-59	45 226	5.1	11	0.02	46 509	5.9	7	0.02	1.6 (0.6-4.2)
60-64	28 809	3.3	2	0.01	30 118	3.8	3	0.01	0.7 (0.1-4.2)
≥65	24 954	2.8	3	0.01	25 580	3.2	4	0.02	0.8 (0.2-3.4)
Risk category									
High	23 176	2.6	1129	4.87	13 685	1.7	445	3.25	
Intermediate	43 315	4.9	221	0.51	25 884	3.3	93	0.36	
Low	814 042	92.4	123	0.02	752 068	95.0	126	0.02	

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus.

donors. The proportions of available HIV-seropositive donations in each period were consistent across demographic subcategories, indicating no selection bias. Since each first-time donation represents an individual donor, the occurrence of new infec-

tions in the 311-day (95% CI, 217-483 days) window period of the less-sensitive EIA protocol[4] could be projected into an incidence rate and residual risk of HIV-1 transmission.[10]

Between 1999-2000 and 2001-2002 the incidence of HIV-1 among first-

time donors declined from 229 to 95 per 100 000 person-years (RR, 2.4; 95% CI, 1.6-3.2), resulting in a 58% decrease in residual risk from 9.4 to 3.9 infectious units per 100 000 donations. The proportion of recent HIV-1 infections decreased from 18% to 14%

Table 2. Human Immunodeficiency Virus 1 Prevalence, Incidence, and Residual Risk in First-Time Donors in 1999-2000 and 2001-2002

Donation Groups	Total Donations Screened	No. (%) of HIV-Positive Donors	Samples Available for LS-EIA	No. (%) of Recent Infections	Projected Incidence Rate per 100 000 Person-Years (95% CI)	Residual Risk per 100 000 Donors (95% CI)	Risk Ratio Between Years (95% CI)
All first-time donors							
1999-2000	93 378	1006 (1.08)	674	122 (18)	229 (123.5-334.6)	9.4 (4.7-14.1)	2.4 (1.6-3.2)
2001-2002	67 231	398 (0.59)	379	52 (14)	95 (47.1-143.7)	3.9 (1.8-6.0)	
Sex							
1999-2000							
Men	48 539	419 (0.86)	296	51 (17)	175 (86.6-262.8)	7.2 (3.3-11.0)	2.3 (1.1-3.4)
Women	44 839	587 (1.31)	378	71 (19)	289 (149.3-428.3)	11.9 (5.7-18.0)	2.5 (1.5-3.5)
2001-2002							
Men	34 537	176 (0.51)	165	21 (13)	76 (30.2-122.2)	3.1 (1.2-5.1)	
Women	32 692	222 (0.68)	214	31 (14)	115 (81.6-179.5)	4.7 (2.0-7.5)	
Geography							
1999-2000							
Free state	10 621	158 (1.49)	102	24 (24)	411 (175.1-647.1)	16.9 (6.7-27.0)	4.6 (0.2-9.0)
Gauteng	55 118	513 (0.93)	338	55 (16)	178 (89.1-266.6)	7.3 (3.4-11.2)	1.8 (1.0-2.6)
Mpumalanga	12 579	149 (1.18)	107	16 (15)	208 (74.4-341.7)	8.5 (2.8-14.2)	1.4 (0.3-2.6)
Northern Cape	3864	16 (0.41)	13	3 (23)	112 (0-245.4)	4.6 (0-10.1)	2.5 (0-8.0)
Northern Province	1449	7 (0.48)	6	9 (33)	189 (0-457.4)	7.8 (0-18.9)	∞ (0-∞)
North West	9747	163 (1.67)	108	22 (20)	400 (164.9-635.2)	16.4 (6.3-26.5)	3.3 (0.4-6.3)
2001-2002							
Free state	6903	44 (0.64)	42	5 (12)	89 (2.4-175.8)	3.7 (0-7.3)	
Gauteng	39 500	227 (0.57)	216	31 (14)	97 (43.3-150.4)	4 (1.7-6.3)	
Mpumalanga	7703	67 (0.87)	64	9 (14)	144 (31.7-255.6)	5.9 (1.2-10.6)	
Northern Cape	2566	13 (0.51)	13	1 (8)	46 (0-137.6)	1.9 (0-5.7)	
Northern Province	4267	15 (0.35)	12	0 (0)	0 (0-46.7)	0 (0-1.9)	
North West	6292	32 (0.51)	30	6 (20)	119 (11.6-227.3)	4.9 (0.4-9.4)	
Race							
1999-2000							
Black	15 530	905 (5.83)	609	107 (18)	1202 (642.7-1762.3)	49.4 (24.7-74.0)	1.8 (1.2-2.5)
Mixed	5543	61 (1.10)	36	6 (17)	215 (25.2-405.6)	8.8 (0.9-16.8)	2.4 (0-5.9)
White	69 068	36 (0.05)	27	8 (30)	18 (3.8-32.5)	0.7 (0.1-1.4)	1.3 (0-2.6)
Asian	3237	4 (0.12)	2	1 (50)	73 (0-199.6)	3 (0-8.2)	∞ (0-∞)
2001-2002							
Black	8032	321 (4.00)	305	43 (14)	661 (316.9-1006.6)	27.2 (12.2-42.2)	
Mixed	3959	41 (1.04)	41	3 (7)	89 (0-196.7)	3.7 (0-8.1)	
White	52 298	34 (0.07)	32	6 (19)	14 (1.4-27.2)	0.6 (0-1.1)	
Asian	2941	2 (0.07)	1	0 (0)	0 (0-78.3)	0 (0-3.2)	
Risk categories							
1999-2000							
High	18 458	946 (5.13)	632	110 (17)	1047 (561.0-1534.3)	43 (21.6-64.5)	1.9 (1.2-2.5)
Intermediate	2615	20 (0.76)	13	3 (23)	207 (0-449.0)	8.5 (0-18.6)	∞ (0-∞)
Low	72 305	40 (0.06)	29	9 (31)	20 (4.9-35.4)	0.8 (0.2-1.5)	1.5 (0-2.9)
2001-2002							
High	10 125	346 (3.42)	330	46 (14)	559 (271.0-847.9)	23 (10.4-35.5)	
Intermediate	1866	16 (0.86)	16	0 (0)	0 (0-85.9)	0 (0-3.5)	
Low	55 528	36 (0.06)	33	6 (18)	14 (1.4-26.3)	0.6 (0-1.1)	

Abbreviations: CI, confidence interval; LS-EIA, less-sensitive enzyme-linked immunoassay.

Table 3. HIV Prevalence, Incidence, Residual Risk of Infection, and Projected IDNAT Yields for All Donations in 2001-2002

Donation Frequency	Total Donations Screened	No. (%) of HIV-Positive Donations	No. of Samples Available for LS-EIA	No. (%) of Recent Infections	HIV Incidence Rate per 100 000 Donation-Years (95% CI)*	Residual Risk by Screening Strategy per 100 000 Donations (95% CI)		Project Yield of Implementing IDNAT per 100 000 Donations	
						p24 Antigen†	IDNAT†	IDNAT to p24 Antigen‡	IDNAT to HIV Antibody‡
First time	67 231	398 (0.59)	379	52 (14)	95.4 (47.1-143.7)	3.9 (1.8-6.0)	1.5 (0.7-2.2)	2.5 (1.1-3.8)	3.7 (1.7-5.8)
Lapsed	67 262	159 (0.24)	155	35 (23)	62.7 (28.8-96.6)	2.6 (1.1-4.0)	1 (0.4-1.5)	1.6 (0.7-2.6)	2.5 (1.0-3.9)
Repeat	657 150	107 (0.02)	107	83 (78)	60.9 (49.4-72.4)	2.5 (1.8-3.2)	0.9 (0.7-1.2)	1.6 (1.1-2.1)	2.4 (1.7-3.1)
All	791 643	664 (0.08)	641	170 (26)	64 (53.2-74.8)	2.6 (2.0-3.3)	1 (0.8-1.2)	1.6 (1.1-2.1)	2.5 (1.8-3.2)

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; IDNAT, individual donation nucleic acid testing; LS-EIA, less-sensitive enzyme-linked immunoassay.
*First-time and lapsed donor incidence rate is estimated by the proportion of recent infections divided by the mean LS-EIA window period of 311 days (SE 68 days), as derived from Fang et al.[4] Repeat donor incidence rate is estimated by incident infections divided by person-time (ie, 107/[657, 150 × 97]), where the average interdonation interval was 97 days (data not shown). The overall incidence rate is the weighted (weighted by total donations screened) average of the donor type incidence rates.
†Assuming the mean (SE) window period from first HIV viremia to p24 antigen positivity is 15.0 (1.4) days to IDNAT positivity is 5.6 (0.4) days.[10]
‡Assuming the mean (SE) window period from IDNAT positivity to p24 positivity is 9.4 (1.2) days and to antibody positivity is 14.7 (1.5) days.[10]

(P=.07). Taken together, 28% fewer first-time donors were collected, these donors were 45% less likely to be infected with HIV-1, and the infections were 24% less likely to be recent. A breakdown of first-time donors into demographic categories reveals that declines in incidence rates and residual risk were seen in most categories (Table 2), achieving statistical significance in the Gauteng province, the black population, both sex groups and in the high-risk group. The white group was the only category that tended toward an increased HIV-1 prevalence (from 0.05% to 0.07%; P=.40) that was offset by a 37% reduction in recent infections (30% vs 19%).

Residual Risk of Collecting an Infectious HIV-1 Window Period Unit

In 2001-2002, 8.5% of donations each were from first-time and lapsed donors; these donations had a 36-fold and a 15-fold higher prevalence of HIV-1 infection than repeat donations, respectively (**TABLE 3**). Available HIV-1 positive samples from all donations were anonymized and subjected to less-sensitive EIA analysis. As shown in Table 3, 83 (78%) of 107 repeat, 35 (23%) of 155 lapsed, and 52 (14%) of 379 first-time donations were likely collected from donors with recent seroconversion, emphasizing that when HIV-1 infection is detected in repeat or lapsed donors, it is more

likely to represent a recently acquired infection compared with seropositive units from first-time donors.

Although repeat donors contributed the largest number of high-risk recently acquired HIV-1 infections (83 vs 52) from first-time and 35 from lapsed donors), these donors represented the lowest overall frequency (12.6 per 100 000 donations). The residual risk of HIV-1 transmission was derived using the time ratio method developed by Busch et al.[10] Using the current HIV-1 screening regimen, the residual risk of collecting an HIV-1 window-period unit is estimated at 2.6 (95% CI, 2.0-3.3) per 100 000 donations, with the highest rate of 3.9 (95% CI, 1.8-6.8) in first-time donations and the lowest, 2.5 (95% CI, 1.8-3.2) per 100 000, in repeat donations. These data were used to predict that the introduction of universal individual donation nucleic acid testing (IDNAT) would reduce the overall risk by 63%, to 1.0 (95% CI, 0.8-1.2) per 100 000 donations, and with annual collections of 700 000 units, would detect an additional 11.2 (95% CI, 7.7-14.7) viremic antibody-negative donations per year.

COMMENT

South Africa is being ravaged by a growing epidemic of HIV/AIDS that is spreading through every demographic group and now infects over 5 million individuals.[3,4,23] In 2003 the rates of infection in young women attending public antena-

tal clinics in a wide geographic distribution ranged from 13.1% to 37.5%.[23] The prevalence of HIV-1 in this high-risk group provides an annual indicator of HIV-1 expansion in South Africa, given the absence of other reliable population infection data (Figure 1). In this milieu, SANBS has strived to maintain a safe and sufficient blood supply for all South Africans.

The World Health Organization (WHO) estimates that 5% to 10% of HIV/AIDS cases continue to be acquired from infected blood transfusions[18,24] and advocates that each country adopt a national blood policy that embraces voluntary nonremunerated donation by a donor pool that is selected for low risk. Donors should be screened for risk factors, educated to avoid risk behaviors, and encouraged to donate repeatedly, and all donations should be tested for major pathogens. Despite the adoption of these measures in South Africa, the 1990s saw a rapidly rising prevalence of HIV in blood donations, increasing from 0.06% in 1991 to 0.26% in 1998. An analysis of a representative sample of 19 709 donations in 1999 using IDNAT and less-sensitive EIA testing, suggested that 1:29 400 whole blood collections might be contaminated with HIV-1.[4]

In response to this threat, the SANBS adopted a standardized blood safety policy that includes the closure of donation sites with high HIV prevalence, implementation of direct oral questioning using a stringent self-exclusion

questionnaire that incorporates questions about heterosexual and homosexual contacts, and intravenous drug abuse, HIV risk behaviors, and a product triage system based on donation risk profiling. Prevalence of HIV in the donor population declined progressively reaching 0.05% in 2003, in contrast with the persistent increase documented in antenatal clinic attendees (Figure 1).[23] Comparison of the demographic features underpinning the decrease in HIV-1 prevalence showed that fewer first-time donations and fewer high- and intermediate-risk category donations were collected. First-time donors were also less likely to be HIV-1 infected or to have been recently exposed. Our data cannot address whether these declines were predominantly due to better selection or education of donors.

Residual risk for collecting an HIV-1 window-period infectious unit in 2001-2002 was 2.6 per 100 000 donations, an approximate 24% decrease in window-period risk from that estimated in 1999 by Fang et al,[4] despite an 18% increase in HIV-1 prevalence in antenatal clinic attendees over that period (Figure 1). Prevalence of HIV-1 in blood donations decreased from 0.19% in 1999[4] to 0.08% in 2001-2002 (a 56% decline) suggesting that SANBS policies were more effective at preventing the collection of donors with established HIV-1 infections that are readily detected using serological tests than recently infected donors who may represent a window-period risk. These estimates are based on the calculated 311-day (95% CI, 217-483 days) window period for the less-sensitive EIA as determined in a relatively small number of donations by Fang et al.[4] The advent of universal IDNAT testing in South Africa now provides an opportunity to validate these estimates and verify the true risks of HIV-1 transmission.

The risk to patients was likely further reduced by SANBS product triage policy that prevented the routine transfusion of cellular products from the high-

and intermediate-risk donation categories that yielded 438 (81%) of 664 donations that tested positive for HIV-1 (Table 1). However, our finding that repeat donations, generally considered to be from individuals at low risk of HIV infection, contributed 83 (48%) of 170 (Table 3) of recent infections, suggests that future risk models should be based on HIV-1 incidence, not prevalence rates. Currently SANBS confirms HIV-1 transfusion transmission in 1 to 2 recipients each year (data not shown).[25]

From a global perspective, South Africa has maintained a safe blood supply by maximizing collections from an ever diminishing repeat donor pool. Average donor frequency increased from 1.8 donations per year in 1998 to 2.8 in 2001, with 65 296 donors supplying half of the 586 089 units collected in the Inland Region of SANBS in 2001.[17] The effect of closing donation sites in high-risk regions has been to skew the donor pool severely so that black individuals who comprise 79% of the population[20] contributed only 4.2% of the blood supply in 2001-2002, down from 10% in 1999.[4] Although these donor selection and product triage policies are effective, they are not sustainable given recent demographic trends. Moreover, concern has been raised with respect to equity, given that cellular products were used selectively and that closing blood donation sites effectively denies donation to blacks who do not indulge in high-risk behavior but donate at clinics located in high-risk areas.[26] These policies have been justified on the basis that safe blood is distributed to all South Africans equally, with the majority black population receiving most (>80%) of the benefit of a safe blood supply, and that all donors can contribute to the blood supply in some way. Even high-risk donors can contribute plasma for transfusion if they are found to be acceptable on a subsequent donation.

There has nevertheless been a strong motivation to develop donor screening systems that identify heterosexual behaviors that place prospective donors at increased HIV-1 risk and to end

the practice of donation risk profiling using race as a marker. Risk markers described in other African countries include first-time donation, age older than 25 years, being married, paying for sex, recruitment venue, sexually transmitted disease or genital ulcer history, condom use, incarceration, and multiple sex partners.[27-32] Many of these markers are included in the current self-exclusion questionnaire but have been ineffective at preventing high-risk donations to date.

In December 2004, the use of race as a risk indicator was found to be unacceptable by the South African Department of Health. Negotiations between SANBS and the Minister of Health led to the implementation in October 2005 of a new Donor Status Risk Management Policy underpinned by IDNAT testing. This policy continues to use stringent donor selection, universal testing, and product triage to ensure blood safety; however, race and sex are no longer criteria for including or excluding blood donors.

To identify behavioral risk profiles while collecting blood in populations known to harbor HIV-1 risk, HIV-1 incident infections must be identified in real time. To this end, and to interdict window-phase units, SANBS implemented IDNAT testing for HIV-1 and hepatitis B and C of all donations in early October 2005 and concurrently began to promote repeated blood donation in the black population. At the time of implementation, IDNAT is expected to yield an additional 11.2 (95% CI, 7.7-14.7) viremic, seronegative donations per year and to reduce window period risk by at least 63% to 1.0 infective unit per 100 000 transfused components (assuming 100% transmission by units collected during the 5.6-day residual infectious window period preceding the IDNAT detection threshold). This risk may increase as the donor base is broadened, with IDNAT yield moderating increased HIV-1 incidence.

Under the new triage policy, fresh frozen plasma is quarantined and only released for transfusion if the subsequent

donation tests negative for infectious markers as before. Platelet components are made only from donors who have donated on 4 or more occasions in the prior 24 months. Red blood cells from first-time donors are segregated and used only when there is a shortage of blood. Prevalence of HIV-1, incidence, and residual risk will be closely monitored and reported as changes are implemented. It is likely that further refinements to both the donor selection and product triage policies will be made as risks are identified.

In the long term, we believe that education of blood donors will be a key factor for ongoing blood safety. There is a need for a structured program that is culturally attuned and presented in the multiple languages in common use.[20] SANBS has been awarded funding under the President's Emergency Plan for AIDS Relief to work with the Centers for Disease Control and Prevention, the American Association of Blood Banks, and the American Red Cross to this end. It will be important to link this initiative to a broader national HIV/AIDS program and to promote blood donation as part of a safe lifestyle to prevent the spread of HIV through blood transfusions and high-risk behaviors.

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